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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/821,694	03/28/2001	William Daniel Hillis	0450-0001	9199

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EXAMINER
LU, FRANK WEI MIN

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 05/02/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/821,694	HILLIS, WILLIAM DANIEL	
	Examiner	Art Unit	
	Frank W Lu	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 August 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-114* is/are pending in the application.

4a) Of the above claim(s) *3,4,16,17,26,32,33 and 36-114* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,5-15,18-25,27-31 and 36-39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *28 March 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Response to Amendment

1. Applicant's response to the office action filed on January 6, 2002 has been entered. The claims pending in this application are claims 1-114 with claims 40-114 withdrawn from consideration as the result of the restriction requirement Rejection and/or objection not reiterated from the previous office action are hereby withdrawn. Since amended claims 34 and 35 are dependent on claim 33 and claim 33 is a non-elected claim, claims 34 and 35 are also non-elected. Therefore, claims 1, 2, 5-15, 18-25, 27-31, and 36-39 will be examined.

Election/Restriction

2. This application contains claims 40-114 drawn to an invention nonelected with traverse in the response filed on August 19, 2002. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Claim Objections

3. Claim 5 is objected to because of the following informalities: (1) "-complementary" in line 2 should be "complementary"; and (2) the phrase "the null hybridizing sequence is base" in line 4 should be "the null hybridizing sequence is a base".

4. Claim 20 is objected to because of the following informality: "an RNA" should be "a RNA".

Appropriate correction is required.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 1, 2, 5-15, 18-25, 27-31, and 36-39 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Note that claims 2, 5-15, 18-25, 27-31, and 36-39 are dependent on claim 1.

7. Claim 1 is rejected as vague and indefinite in view of the phrase "wherein each of the at least two oligonucleotide probes has one nucleotide capable of base pairing with a set of two or more nucleotides, said set of two or more nucleotides including one nucleotide common to all sets and lacking one nucleotide present in the target sequence segment" because it is unclear what it intended. Since the first part of the phrase only describes "a set", there is insufficient antecedent basis for "all sets" in the phrase. Please clarify.

8. Claim 2 is rejected as vague and indefinite in view of the phrase "each oligonucleotide probe comprising, at a position corresponding to the position of interest, a nucleotide base pairing with two of four nucleotides present in the target sequence segment" because it is unclear how a nucleotide base at a position corresponding to the position of interest in each oligonucleotide can pair with two of four nucleotides present in the target sequence segment in the same time. Please clarify.

9. Claim 5 is rejected as vague and indefinite in view of the phrase "wherein the null hybridizing sequence is base paired with a set of two or more nucleotides at a variable position of the target sequence segment; and wherein a nucleotide represented in neither a first or second set of the two or more nucleotides at the variable position is used to probe the target sequence segment" because it is unclear what it intended. First, it is unclear how a base (the null hybridizing sequence) can base pair with two or more nucleotides at a variable position of the target sequence segment in the same time. Second, since the first part of the phrase only describes " a set", there is insufficient antecedent basis for "a first or second set" in the phrase. Please clarify.

10. Claim 18 is rejected as vague and indefinite because it is unclear what it intended because a polymerase enzyme itself does not require a hybridized complex. Please clarify.

11. Claim 31 recites the limitation "the linker moiety" in the claim. There is insufficient antecedent basis for this limitation in the claim since there is no linker moiety in claims 1, 6, 7, 9, 14, and 15.

Claim Rejections - 35 USC § 102

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (e) the invention was described in-
> (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effect under this subsection of a national application published under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language; or

(2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a).

13. Claims 1, 6,18, 19, 23, and 24 are rejected under 35 U.S.C. 102(e) as being anticipated by Senapathy (US Paten No. 6,521,428, filed on November 4, 1999).

Note that this rejection was made in view of the ambiguity of claim 1.

Senapathy teaches shot-gun sequencing and amplification without cloning.

Regarding claims 1, 23, and 24, in the method of sequencing a nucleic acid template, the method steps comprised: (a) providing a plurality of first primers, each first primer comprising (I) a region of different fixed nucleotide sequence having a defined length of from about 5 to 15 bases long and (ii) a region of randomized nucleotide sequence having a defined length of from about 2 to 11 bases long located 5' to or 3' to the region of fixed nucleotide sequence and a handle at an end of each first primer wherein the handle was one or more universal bases ; (b) annealing the plurality of first primers to different locations on a nucleic acid template (ie., genomic DNA or cDNA), wherein at least one primer from within the plurality of first primers annealed specifically to the template; (c) extending the specifically annealed primer from step b) with a mixture of dNTPs and ddNTPs to generate a series of nucleic acid fragments; and (d) determining the nucleotide sequence of a first region of the template from the series of nucleic acid fragments (see first paragraph in column 5 and claims 19-24 in columns 25 and 26). Since each first primer comprises a region of different fixed nucleotide sequence having a defined length of from about 5 to 15 bases long, a region of randomized nucleotide sequence having a defined length of from about 2 to 11 bases long located 5' to or 3' to the region of fixed nucleotide sequence and a handle

at an end of each first primer wherein the handle is one or more universal bases and the universal base is capable of base pairing with either a purine or pyrimidine, two first primers are two oligonucleotide probes having one nucleotide capable of base pairing with a set of two or more nucleotides as recited in claim 1. Since at least two first primers anneal to different locations on a nucleic acid template, there is no mismatch to be existed at the position of interest as recited in claim 1. Therefore, claim 1 is anticipated by Senapathy. Since genomic DNA or cDNA are used as a nucleic acid template, claims 23 and 24 are anticipated by Senapathy.

Regarding claim 6, since the method taught by Senapathy is used for sequencing a nucleic acid template, claim 6 is anticipated by Senapathy.

Regarding claims 18 and 19, in the method for amplifying a nucleic acid template, the method steps comprised: (a) providing a plurality of first primers, each first primer comprising (I) a region of different fixed nucleotide sequence having a defined length of from about 5 to 15 bases long and (ii) a region of randomized nucleotide sequence having a defined length of from about 2 to 11 bases long located 5' to or 3' to the region of fixed nucleotide sequence; (b) providing a plurality of second primers, each second primer comprising (I) a region of different fixed nucleotide sequence having a defined length of from about 5 to 15 bases long and (ii) a region of randomized nucleotide sequence having a defined length of from about 2 to 11 bases long located 5' to or 3 ' to the region of fixed nucleotide sequence, wherein the regions of fixed nucleotide sequence in the second plurality of primers was shorter than the regions of fixed nucleotide sequence in the first plurality of primers; and (c) amplifying a first region of the nucleic acid template with the plurality of first primers and the plurality of second primers, wherein at

least one primer from within each of the plurality of first primers and the plurality of second primers annealed specifically to the template (see lines 5-15 in column and claim 25 in column 26). Since a polymerase chain reaction is performed in the presence of a polymerase using at least a pair of primers, claims 18 and 19 are anticipated by Senapathy.

Therefore, Senapathy teaches all limitations recited in claims 1, 6, 18, 19, 23, and 24.

Claim Rejections - 35 USC § 103

14. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

15. Claims 21 and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Senapathy (1999) as applied to claims 1, 6, 18, 19, 23, and 24 above, and further in view of Santamaria *et al.,* (US Patent No.5, 578, 443, published on November 26, 1996).

The teachings of Senapathy have been summarized previously, *supra.*

Senapathy does not disclose to use his method for a genetic analysis such as allelic analysis as recited in claims 21 and 22.

Santamaria *et al.,* teach DNA sequence-based HLA typing method. Their PCR and sequencing methods were used for a genetic analysis such as allelic analysis (see lines 9-47 in column 2 and lines 14-21 in column 4).

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have used the method recited in claim 1 for a genetic analysis (ie., allelic analysis) in view of the patents of Senapathy and Santamaria *et al.*. One having ordinary skill in the art would have been motivated to do so because Santamaria *et al.*, have successfully used a sequencing method for a genetic analysis (ie., allelic analysis) and the simple replacement of one kind of sequencing method (i.e., the sequencing method taught by Santamaria *et al.*,) from another kind of sequencing method (i.e., the sequencing method taught by Senapathy) for a genetic analysis would have been, in the absence of convincing evidence to the contrary, *prima facie* obvious to one having ordinary skill in the art at the time the invention was made because the replacement would not change the experimental results.

Furthermore, the motivation to make the substitution cited above arises from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combined for their common known purpose. Support for making the obviousness rejection comes from the M.P.E.P. at 2144.07 and 2144.09.

Also note that there is no invention involved in combining old elements is such a manner that these elements perform in combination the same function as set forth in the prior art without giving unobvious or unexpected results. *In re Rose* 220 F.2d. 459, 105 USPQ 237 (CCPA 1955).

Conclusion

16. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

17. No claim is allowed.

18. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CAR § 1.6(d)). The CM Fax Center number is either (703) 308-4242 or (703)305-3014.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frank Lu, Ph.D., whose telephone number is (703) 305-1270. The examiner can normally be reached on Monday-Friday from 9 A.M. to 5 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion, can be reached on (703) 308-1119.

Any inquiry of a general nature or relating to the status of this application should be directed to the patent Analyst of the Art Unit, Ms. Chantae Dessau, whose telephone number is (703) 605-1237.

Frank Lu
May 1, 2003

Ethan Whisenant, Ph.D.
Primary Examiner (FSA)